VACCINES OF THE FUTURE

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Rio de Janeiro, Brazil, 26 August 2010
PLAN OF THE TALK

• Vaccines of the near future (5-10 years).

• Vaccines of the medium future (10-20 years).

• Vaccines of the long-term future (20-50 years).

• Adjunct issues: combinations, alternative delivery, adjuvants.
VACCINES OF THE NEAR FUTURE (5-10 YEARS)

- Vi-conjugate vaccine for typhoid.
- Protein-based vaccine for *Neisseria meningitidis* serogroup B.
- Common protein vaccine for *Streptococcus pneumoniae*.
- Cheaper variants of rotavirus vaccine.
- Slightly more distant: Shigellosis.
  Group A streptococcus.
Malaria: RTS,S is in phase III trial but will not be the definitive malaria vaccine. Progress is good for other components.

- Genetically attenuated sporozoites (Kappe).
- Liver stage (Chitnis).
- Blood stage (especially AMA1).
- Gametocyte (various antigens).
VACCINES OF THE MEDIUM-TERM FUTURE (10-20 YEARS) II

- Tuberculosis.
  - Prophylactic.
    - Various rBCG in phase I trial.
    - Viral vectored for prime-boost, e.g. MVA-85A or Ad35-85A, 85B, TB10.4, in phase II trial.
    - Recombinant protein, e.g. 85B and ESAT-6 in phase II trial.
  - Therapeutic only.
    - M. vaccae (inactivated) in BCG-primed HIV-positive subjects completed phase III, reformulation pending.
      - In preclinical studies.
    - At least 25 more candidates.

- Clinical trials long and expensive.
Sanofi-Pasteur Rv144 ALVAC-R prime – AIDSVAX gp120 boost phase III trial in 16,000 Thai subjects showed 31.2% efficacy (74 seroconversions versus 51) but no effect on viral load. Follow-on trials will characterize antibodies and seek correlates of protection.

Antibody-based vaccines are not dead. The two key approaches will be studying the binding sites of broadly-neutralizing monoclonal antibodies; and seeking mimotopes of the transition state of gp120 after CD4 binding but before co-receptor binding.

Shaw’s finding that only one or at most a few virions initiate infection gives some hope. Prevention does not need to neutralize a massive viral load.
VACCINES OF THE LONG-TERM FUTURE (20-50 YEARS)

• “Negative” vaccines for autoimmune diseases.
  • Insulin intranasally for pre-diabetes.
  • Ditto peptides and mimotopes to stimulate T-regs.
  • Gluten peptides for coeliac disease.

• Vaccines or monoclonal antibodies for cancer.
  • Most vaccines “fall over” in phase III trials.
  • Ipilimumab (anti-CTLA4 monoclonal) increases median overall survival in phase III study of unresectable Stage III or IV melanoma (NEJM 16 June 2010).
  • Best target for immunotherapy may be minimal residual disease.
ADJUNCT ISSUES

• More extensive combinations.

• Needle-free delivery systems, e.g. transdermal.

• New mucosal approaches.

• New adjuvants based on TLR and other innate receptors.